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## Modeling age at menopause

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on this topic and believe it should be left up to individual centers as to whether they think it is worth pursuing.

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## Modeling age at menopause

*To the Editor:*

From their study, van Asselt et al. (1) report a heritability of 44% for the menopausal age in a Dutch sample of 164 mothers and their daughters. This heritability estimate is based on a familial correlation of 0.22. As noted by the authors, this correlation can be due to either shared genes or shared environment, and the heritability is therefore overestimated if shared environmental factors influence the trait. With twin data, it is possible to disentangle the influences of shared genes and shared environment.

We analyzed data on age at natural menopause from 200 twin–sister pairs from the Netherlands Twin Register (NTR) (2). We had data for 52 monozygotic (MZ) twin pairs and for 148 dizygotic (DZ) and sister (sibling) pairs. Mean age at time of completing the NTR survey was 56.05 years (SD = 5.3). A mean age of 47.3 years (SD = 6.2) for age of menopause was reported, with a 2-year test–retest correlation for age of menopause of .87 ( $P=.000$ ) in a sample of 177 women who completed the survey twice.

The correlation for age at menopause was 0.597 ( $P=.000$ ) for MZ twin pairs and 0.170 ( $P=.039$ ) in the DZ–sister group. This pattern of correlations strongly suggests genetic influences on age at natural menopause. We used structural equation modeling to obtain estimates of the additive genetic (A) and environmental variances (E). We also tested whether

a model that included shared environment explained the data better than an AE model. Results showed that shared environmental influences did not contribute to the variation in age of natural menopause [ $\chi^2(1) = 1.72$ ]. The heritability estimate was 60% (95% confidence interval 37%–91%) for variance in age at natural menopause.

Our result, from a Dutch sample recruited through the NTR, thus is in line with the heritability (44%) based on mother–daughter correlations and the heritability (71%) reported earlier for an independent, somewhat smaller, sample of Dutch twins (3). We can conclude that in the Dutch population, the heritability for age at menopause is approximately 60%. This is in line with other studies that investigated the heritability of the age at natural menopause (4, 5). Because several studies have detected a genetic influence on menopausal age, this suggests that women with a family history of early menopause are at higher risk to experience an early menopause themselves.

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December 8, 2004

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## Technical challenges in freeze–thawing of human ovary

*To the Editor:*

We have read with great interest the recent article on freeze–thawing of intact human ovary with its vascular pedicle by Martinez-Madrid et al. (1). There are some details that are not discussed in the article that are important for understanding their work. We agree that cryopreservation of the entire organ with its vascular pedicle is technically feasible, as we showed in our earlier work (2, 3); however the authors need to address the following points. First, they said the ovary was placed in a cryovial where it was pre-equilibrated,